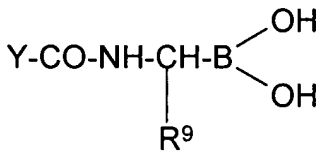
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (original): A parenteral pharmaceutical formulation comprising a therapeutically effective amount of a pharmaceutically acceptable base addition salt of a boronic acid of formula (I):



(I)

wherein

Y comprises a hydrophobic moiety which, together with the aminoboronic acid residue $-NHCH(R^9)-B(OH)_2$, has affinity for the substrate binding site of thrombin; and

R^9 is a straight chain alkyl group interrupted by one or more ether linkages and in which the total number of oxygen and carbon atoms is 3, 4, 5 or 6 or R^9 is $-(CH_2)_m-W$ where m is from 2, 3, 4 or 5 and W is –OH or halogen.

Claim 2 (original): The formulation of claim 1 wherein R^9 is an alkoxyalkyl group.

Claim 3 (original): The formulation of claim 1 wherein YCO- comprises an amino acid residue which binds to the S2 subsite of thrombin, the amino acid residue being N-terminally linked to a moiety which binds the S3 subsite of thrombin.

Claim 4 (original): The formulation of claim 1 wherein Y comprises a dipeptide which binds to the S3 and S2 binding sites of thrombin.

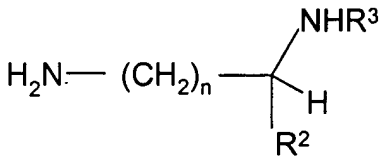
Claim 5 (original): The formulation of claim 4 wherein the S3-binding amino acid residue is of (R)-configuration, the S2-binding residue is of (S)-configuration, and the fragment – NHCH(R^9)-B(OH) is of (R)-configuration.

Claim 6 (currently amended): The formulation of claim ~~4~~ 5 wherein R^9 is an alkoxyalkyl group.

Claim 7 (original): The formulation of claim 1 wherein the boronic acid has a Ki for thrombin of about 100 nM or less.

Claim 8 (original): The formulation of claim 1 wherein the salt comprises a salt of the boronic acid with metal or a strongly basic organic nitrogen-containing compound.

Claim 9 (original): The formulation of claim 1 wherein the salt comprises a salt of the boronic acid with an alkali metal, an aminosugar, a guanidine or an amine of formula (XI):



(XI)

where n is from 1 to 6, R^2 is H, carboxylate or derivatised carboxylate, R^3 is H, C_1-C_4 alkyl or a residue of a natural or unnatural amino acid.

Claim 10 (original): The formulation of claim 4 wherein the Y dipeptide is N-terminally protected or N-terminally unprotected, and the peptide linkages in the dipeptide are unsubstituted or independently N-substituted by a C_1-C_{13} hydrocarbyl, wherein the C_1-C_{13} hydrocarbyl contains no heteratoms or at least one in-chain or in-ring nitrogen, oxygen or sulfur atom, and the C_1-C_{13} hydrocarbyl is unsubstituted or substituted by a substituent selected from halo, hydroxy and trifluoromethyl.

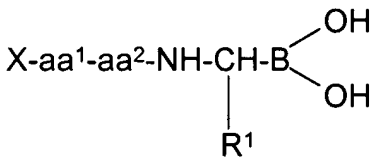
Claim 11 (original): The formulation of claim 1 wherein the salt consists essentially of an acid salt in which one B-OH group of formula (I), when trigonally represented, remains protonated.

Claim 12 (original): The formulation of claim 9 wherein the salt comprises boronate ions derived from the peptide boronic acid and has a stoichiometry consistent with the boronate ions carrying a single negative charge.

Claim 13 (original): The formulation of claim 6 wherein the salt consists essentially of a monosodium or monolithium salt of the boronic acid.

Claim 14 (original): The pharmaceutical formulation of claim 9 which is adapted for intravenous administration.

Claim 15 (original): A formulation in parenteral dosage form comprising a therapeutically effective amount of a pharmaceutically acceptable base addition salt of a boronic acid of formula (II):



(II)

where:

X is H or an amino-protecting group;

aa^1 is an amino acid residue having a hydrocarbyl side chain containing no more than 20 carbon atoms and comprising at least one cyclic group having up to 13 carbon atoms;

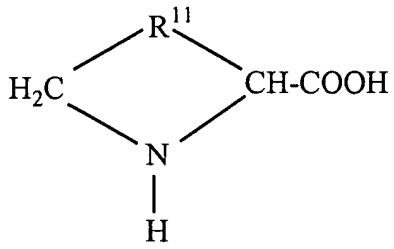
aa^2 is an imino acid residue having from 4 to 6 ring members;

R^1 is a group of the formula $-(CH_2)_s-Z$, where s is 2, 3 or 4 and Z is –OH, –OMe, –OEt or halogen.

Claim 16 (currently amended): The formulation of claim 15 wherein aa^1 is selected from Phe, Dpa ~~and~~ or wholly or partially hydrogenated analogues thereof.

Claim 17 (original): The formulation of claim 16 wherein aa^1 is of R-configuration.

Claim 18 (original): The formulation of claim 15 wherein aa^2 is a residue of an imino acid of formula (IV)



(IV),

where R^{11} is $-CH_2-$, $-CH_2-CH_2-$, $-S-CH_2-$, $-S-C(CH_3)_2-$ or $-CH_2-CH_2-CH_2-$, and, when the formula (IV) ring is 5- or 6- membered, the formula (IV) ring is unsubstituted or is substituted at one or more $-CH_2-$ groups by from 1 to 3 C_1-C_3 alkyl groups.

Claim 19 (original): The formulation of claim 18 wherein aa^2 is of S-configuration.

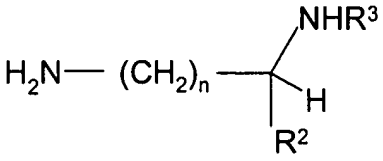
Claim 20 (original): The formulation of claim 15, wherein aa^1-aa^2 is (R)-Phe-(S)-Pro and the fragment $-NH-CH(R^1)-B(OH)_2$ is of R-configuration.

Claim 21 (original): The formulation of claim 16 wherein the boronic acid is of formula (VIII):

X-(R)-Phe-(S)-Pro-(R)-Mpg-$B(OH)_2$(VIII),

wherein X is R^6-$(CH_2)_p$-C(O)-, R^6-$(CH_2)_p$-S(O)$_2$-, R^6-$(CH_2)_p$-NH-C(O)- or R^6-$(CH_2)_p$-O-C(O)- wherein p is 0, 1, 2, 3, 4, 5 or 6 and R^6 is H or a 5 to 13-membered cyclic group which is unsubstituted or substituted by 1, 2 or 3 substituents selected from halogen; amino; nitro; hydroxy; a C_5-C_6 cyclic group; C_1-C_4 alkyl and C_1-C_4 alkyl containing, or linked to the cyclic group through, an in-chain O atom, the aforesaid alkyl groups optionally being substituted by a substituent selected from halogen, amino, nitro, hydroxy and a C_5-C_6 cyclic group.

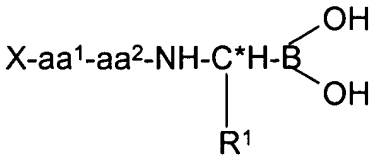
Claim 22 (original): The formulation of claim 16 wherein the salt comprises a salt of the boronic acid with an alkali metal, an aminosugar or an amine of formula (XI):



(XI)

where n is from 1 to 6, R^2 is H, carboxylate or derivatised carboxylate, R^3 is H, C_1-C_4 alkyl or a residue of a natural or unnatural amino acid.

Claim 23 (original): A pharmaceutical product comprising a sealed container containing in the form of a finely divided solid, ready for reconstitution to form a liquid parenteral formulation, a therapeutically effective amount of a boronate salt which consists essentially of a single pharmaceutically acceptable base addition salt of a boronic acid formula (II):



(II)

where:

X is H or an amino-protecting group;

aa^1 is an amino acid residue of R-configuration having a hydrocarbyl side chain containing no more than 20 carbon atoms and comprising at least one cyclic group having up to 13 carbon atoms;

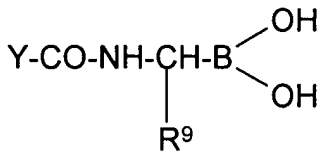
aa^2 is an imino acid residue of S-configuration having from 4 to 6 ring members;

C* is a chiral centre of R-configuration; and

R^1 is a group of the formula $-(CH_2)_s-Z$, where s is 2, 3 or 4 and Z is –OH, –OMe, –OEt or halogen.

Claim 24 (currently amended): A pharmaceutical formulation adapted for parenteral administration, whether directly or after combining with a liquid, and comprising

a) a first species selected from a boronic acid of formula (I), and boronate ions of said boronic acid and equilibrium forms of said boronic acid and said boronate ions:



(I)

wherein
Y comprises a hydrophobic moiety which, together with the aminoboronic acid residue $-NHCH(R^9)-B(OH)_2$, has affinity for the substrate binding site of thrombin; and

R^9 is a straight chain alkyl group interrupted by one or more ether linkages and in which the total number of oxygen and carbon atoms is 3, 4, 5 or 6 or R^9 is $-(CH_2)_m-W$ where m is from 2, 3, 4 or 5 and W is –OH or halogen; and

(b) a second species selected from pharmaceutically acceptable metal ions, said metal ions having a valency of n, lysine, arginine ~~and~~ or aminosugars,

wherein the formulation has an observed stoichiometry of first to second species essentially consistent with a notional stoichiometry of 1:1 when the second species is a metal ion with a valency of 1 or is lysine, arginine or an aminosugar, or an observed stoichiometry of n:1 when the second species is a metal ion with a valency of greater than 1.

Claim 25 (original): A method of inhibiting thrombin in the prophylaxis or therapy of disease, comprising parenterally administering to a mammal suffering from, or at risk of suffering from, thrombosis a therapeutically effective amount of the salt defined in claim 1.

Claim 26 (original): A method for preventing thrombosis in a haemodialysis circuit of a patient, for preventing a cardiovascular event in a patient with end stage renal disease, for preventing venous thromboembolic events in a patient receiving chemotherapy through an indwelling catheter, for preventing thromboembolic events in a patient undergoing a lower limb arterial reconstructive procedure, or for treating by way of therapy or prophylaxis an arterial disease selected from acute coronary syndromes, cerebrovascular thrombosis, peripheral arterial occlusion and arterial thrombosis resulting from atrial fibrillation, valvular heart disease, arterio-venous shunts, indwelling catheters or coronary stents, the method comprising parenterally administering to a mammal a therapeutically effective amount of the salt defined in claim 16.

Claim 27 (original): A method for making a salt of claim 1, comprising:

combining in a solvent diethanolamine and an ester of a boronic acid as defined in claim 1;

allowing or causing a precipitate to form and recovering the precipitate;

converting the precipitated material into the free organoboronic acid by contacting the precipitated material with an aqueous acid or base; and

reacting the organoboronic acid with a base of a pharmaceutically acceptable multivalent metal to form to a salt as defined in claim 1.

Claim 28 (original): A medicament adapted for parenteral administration and comprising a therapeutically effective amount of a pharmaceutically acceptable base addition salt of a boronic acid which is a selective thrombin inhibitor and has a neutral aminoboronic acid residue capable of binding to the thrombin S1 subsite linked through a peptide linkage to a hydrophobic moiety capable of binding to the thrombin S2 and S3 subsites, the salt comprising a cation having a valency n and having an observed stoichiometry consistent with a notional stoichiometry (boronic acid:cation) of n:1.

Claim 29 (original): A medicament of claim 28 wherein the boronic acid has a Ki for thrombin of about 100 nM or less.

Claim 30 (new): The method of claim 25, wherein the boronic acid is of formula (VIII):

X-(R)-Phe-(S)-Pro-(R)-Mpg-$B(OH)_2$(VIII),

wherein X is R^6-$(CH_2)_p$-C(O)-, R^6-$(CH_2)_p$-$S(O)_2$-, R^6-$(CH_2)_p$-NH-C(O)- or R^6-$(CH_2)_p$-O-C(O)- wherein p is 0, 1, 2, 3, 4, 5 or 6 and R^6 is H or a 5 to 13-membered cyclic group which is unsubstituted or substituted by 1, 2 or 3 substituents selected from halogen; amino; nitro; hydroxy; a C_5-C_6 cyclic group; C_1-C_4 alkyl and C_1-C_4 alkyl containing, or linked to the cyclic group through, an in-chain O atom, the aforesaid alkyl groups optionally being substituted by a substituent selected from halogen, amino, nitro, hydroxy and a C_5-C_6 cyclic group.

Claim 31 (new): The method of claim 30, wherein X is R^6-$(CH_2)_p$-O-C(O)-.

Claim 32 (new): The method of claim 31, wherein R^6 is a 6-membered cyclic group that is unsubstituted and p is 1.

Claim 33 (new): The method of claim 25, wherein the salt is an alkali metal salt.

Claim 34 (new): The method of claim 33, wherein the alkali metal salt is a sodium salt.

Claim 35 (new): The method of claim 26, wherein the boronic acid is of formula (VIII):

X-(R)-Phe-(S)-Pro-(R)-Mpg-$B(OH)_2$(VIII),

wherein X is R^6-$(CH_2)_p$-C(O)-, R^6-$(CH_2)_p$-$S(O)_2$-, R^6-$(CH_2)_p$-NH-C(O)- or R^6-$(CH_2)_p$-O-C(O)- wherein p is 0, 1, 2, 3, 4, 5 or 6 and R^6 is H or a 5 to 13-membered cyclic group which is unsubstituted or substituted by 1, 2 or 3 substituents selected from halogen; amino; nitro; hydroxy; a C_5-C_6 cyclic group; C_1-C_4 alkyl and C_1-C_4 alkyl containing, or linked to the cyclic group through, an in-chain O atom, the aforesaid alkyl groups optionally being substituted by a substituent selected from halogen, amino, nitro, hydroxy and a C_5-C_6 cyclic group.

Claim 36 (new): The method of claim 35, wherein X is R^6-$(CH_2)_p$-O-C(O)-.

Claim 37 (new): The method of claim 36, wherein R^6 is benzyloxycarbonyl.

Claim 38 (new): The method of claim 26, wherein the salt is an alkali metal salt.

Claim 39 (new): The method of claim 38, wherein the alkali metal salt is a sodium salt.

Claim 40 (new): The formulation of claim 21, wherein X is R^6-$(CH_2)_p$-O-C(O)-.

Claim 41 (new): The formulation of claim 40, wherein R^6 is benzyloxycarbonyl.

Claim 42 (new): The formulation of claim 21, wherein the formulation is an aqueous solution comprising the salt.

Claim 43 (new): The formulation of claim 42, wherein the aqueous solution further comprises a tonicity agent.

Claim 44 (new): The formulation of claim 42, wherein the salt is an alkali metal salt.

Claim 45 (new): The formulation of claim 44, wherein the alkali metal salt is a sodium salt.

Claim 46 (new): The formulation of claim 1, wherein the formulation comprises an aqueous solution of the salt.

Claim 47 (new): A method of inhibiting thrombin in the prophylaxis or therapy of disease, comprising parenterally administering to a mammal suffering from, or at risk of suffering from, thrombosis, the formulation of claim 1.

Claim 48 (new): The method of claim 47, wherein the boronic acid is of formula (VIII):

X-(R)-Phe-(S)-Pro-(R)-Mpg-$B(OH)_2$(VIII),

wherein X is R^6-$(CH_2)_p$-C(O)-, R^6-$(CH_2)_p$-$S(O)_2$-, R^6-$(CH_2)_p$-NH-C(O)- or R^6-$(CH_2)_p$-O-C(O)- wherein p is 0, 1, 2, 3, 4, 5 or 6 and R^6 is H or a 5 to 13-membered cyclic group which is unsubstituted or substituted by 1, 2 or 3 substituents selected from halogen; amino; nitro; hydroxy; a C_5-C_6 cyclic group; C_1-C_4 alkyl and C_1-C_4 alkyl containing, or linked to the cyclic group through, an in-chain O atom, the aforesaid alkyl groups optionally being substituted by a substituent selected from halogen, amino, nitro, hydroxy and a C_5-C_6 cyclic group.

Claim 49 (new): The method of claim 48, wherein the formulation is an aqueous solution comprising the salt.

Claim 50 (new): The method of claim 49, wherein the formulation is administered intravenously.

Claim 51 (new): A method for preventing thrombosis in a haemodialysis circuit of a patient, for preventing a cardiovascular event in a patient with end stage renal disease, for preventing venous thromboembolic events in a patient receiving chemotherapy through an indwelling catheter, for preventing thromboembolic events in a patient undergoing a lower limb arterial reconstructive procedure, or for treating by way of therapy or prophylaxis an arterial disease selected from acute coronary syndromes, cerebrovascular thrombosis, peripheral arterial occlusion and arterial thrombosis resulting from atrial fibrillation, valvular heart disease, arterio-venous shunts, indwelling catheters or coronary stents, the method comprising parenterally administering to a mammal the formulation of claim 16.

Claim 52 (new): The method of claim 51, wherein the boronic acid is of formula (VIII):

X-(R)-Phe-(S)-Pro-(R)-Mpg-$B(OH)_2$(VIII),

wherein X is R^6-$(CH_2)_p$-C(O)-, R^6-$(CH_2)_p$-$S(O)_2$-, R^6-$(CH_2)_p$-NH-C(O)- or R^6-$(CH_2)_p$-O-C(O)- wherein p is 0, 1, 2, 3, 4, 5 or 6 and R^6 is H or a 5 to 13-membered cyclic group which is unsubstituted or substituted by 1, 2 or 3 substituents selected from halogen; amino; nitro; hydroxy; a C_5-C_6 cyclic group; C_1-C_4 alkyl and C_1-C_4 alkyl containing, or linked to the cyclic group through, an in-chain O atom, the aforesaid alkyl groups optionally being substituted by a substituent selected from halogen, amino, nitro, hydroxy and a C_5-C_6 cyclic group.

Claim 53 (new): The method of claim 52, wherein the formulation is an aqueous solution comprising the salt.

Claim 54 (new): The method of claim 53, wherein the formulation is administered intravenously.

Claim 55 (new): The method of claim 25, further comprising co-administering a cardiovascular treatment agent.

Claim 56 (new): The method of claim 26, further comprising co-administering a cardiovascular treatment agent.

Claim 57 (new): A method of inhibiting thrombin in the prophylaxis or therapy of disease, comprising parenterally administering to a mammal suffering from, or at risk of suffering from, thrombosis a therapeutically effective amount of the pharmaceutical formulation of claim 24.